

REMARKS

Claims 39-40, 46, 47 and 49-55 are pending after this amendment and claims 41-45 have been canceled without prejudice. Applicants expressly reserve the right to pursue the canceled subject matter in this application or subsequent applications that claim the benefit of this application.

Applicants have amended claim 39 to recite that the biological activity is selected from the group consisting of: receptor binding activities, signaling transduction activities, cellular responses induced by PTN, promoting cancer cell growth, promoting cancer cell proliferation, promoting metastasis of cancer cells, and promoting angiogenesis. Support for this amendment can be found, for example, at page 15, lines 8-15 and pages 27-32 and original claims 3-6.

Applicants have amended claim 40 to reverse the order of (a) and (b) as the Examiner suggested.

Applicants have amended claims 40, 46, and 52 to recite a sequence comprising SEQ ID NOs: 5, 6, 7, 10, 11, and 12, or SEQ ID NOs: 3 and 8. Support for this amendment can be found, for example, at page 17, lines 1-7.

Applicants have amended claim 47 to recite an amino acid sequence comprising SEQ ID NOs: 3 and 8. Support for this amendment can be found, for example, at page 17, lines 1-3.

Applicants have amended claim 55 to recite a PTN protein. Support for this amendment can be found, for example, at page 24, lines 12-14 and originally filed claim 34.

No new matter has been introduced. Applicants respectfully request reconsideration in view of the following remarks. The Examiner's rejections and comments are addressed below in the order they were raised in the Office Action.

DETAILED ACTION

Applicants note with appreciation that the response filed January 16, 2008 has been entered.

Claim Rejections under 35 U.S.C. § 112, first paragraph

1. The Examiner has objected to the specification and claim 40 as allegedly failing to provide an adequate written description and failing to provide an enabling disclosure. The Examiner argues that the specification does not provide evidence that the claimed biological materials are (1) known; (2) reproducible from the written description; or (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809. Specifically, the claim allegedly requires the 3B10, 4B2, 10, 17, 24, 25, 26, 27, 31, 41, 50, 60, 87, 3-4A, and 3-11F antibodies.

Applicants request that this objection be held in abeyance. An acceptable deposit of the hybridomas will be made complying with all the proper conditions, assurances, and corroborations to satisfy the criteria set forth in 37 CFR §§ 1.801-1.809 within the required time.

2. The Examiner has objected to the specification and claims 39-47, 49-51 and 53-55 as allegedly failing to provide an adequate written description and failing to provide an enabling disclosure. The Examiner argues that the specification does not provide evidence that the claimed biological materials are (1) known; (2) reproducible from the written description; or (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809. Specifically, the claim allegedly requires the AL1 and either AL12 or AL13 antibodies.

Applicants request that this objection also be held in abeyance. An acceptable deposit of the hybridomas will be made complying with all the proper conditions, assurances, and corroborations to satisfy the criteria set forth in 37 CFR §§ 1.801-1.809 within the required time.

3. Claims 40, 46, 47, and 52 are rejected under 35 USC §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate with that as claimed.

Applicants respectfully disagree. However, in an effort to expedite prosecution of the application, the claims have been amended obviating the rejection. In particular, the claims have

been amended to specify a sequence comprising SEQ ID NOs: 5, 6, 7, 10, 11, and 12, or SEQ ID NOs: 3 and 8. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 112, second paragraph

4. Claims 39-47, 49-51 and 53-55 are rejected under 35 USC 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that in claim 39, and claims dependent thereupon, it is not clear what applicant intends as encompassed by a "biological activity". Applicants respectfully traverse.

The term a "biological activity" is described in the specification in such a way as to be clear to one of ordinary skill in the art. Specifically, a "biological activity" is described in the therapeutic uses section of the specification (see page 15, lines 8-15 and pages 27-32). Each of the activities described in this section is a biological activity of PTN. Nonetheless, solely to expedite prosecution, applicants have amended claim 39 to recite that the biological activity is selected from the group consisting of: receptor binding activities, signaling transduction activities, cellular responses induced by PTN, promoting cancer cell growth, promoting cancer cell proliferation, promoting metastasis of cancer cells, and promoting angiogenesis.

5. The Examiner alleges that claim 40 is vague in the absence of recitation of deposit accession numbers to clearly identify the claimed antibody/hybridoma species and that "the monoclonal antibody" lacks antecedent basis and it is unclear what is within the metes and bounds of the invention because it is not clear what applicant intends as encompassed by "substantially" the same epitope.. Applicants respectfully traverse.

Applicants request that the recitation of deposit accession number be held in abeyance as discussed *supra*. An acceptable deposit will be made before the date of payment of the issue fee.

Applicants do not believe there is an antecedent basis problem with the recited phrase as it refers to the epitope described subsequently. Nevertheless, solely to expedite prosecution, applicants have amended the claim to reverse the order of (b) and (a) as the Examiner suggested.

With regards to the meaning of the term "substantially" the MPEP 2173.05(b) states:

The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.

Applicants respectfully remind the Examiner that according to the MPEP claim language that is acceptable if one of ordinary skill in the art would be able to understand what is claimed in light of the specification. Here the specification provides sufficient guidance to one of ordinary skill for interpreting the claims. The term "substantially the same epitope" as used in claim 40 is clearly defined in the specification as when "amino acid mutations in the protein that reduce or eliminate binding of one antibody also reduce or eliminate binding of the other antibody, and/or if the antibodies compete for binding to the protein, i.e., binding of one antibody to the protein reduces or eliminates binding of the other antibody" (see page 8, lines 10-23). The specification further provides methods of making this analysis such as a competition assay. As required by the MPEP, in light of the specification, one of ordinary skill in the art would understand the claimed subject matter.

This standpoint is further consistent with the same MPEP section, which particularly listed the use of the word "substantially" as being definite if a skilled artisan would be reasonably apprised of the meaning of the term, especially in view of the guidelines set forth in the specification. *See, In re Nehrenberg*, 280 F.2d 161, 126 USPQ 383 (CCPA 1960). In *In re Mattison*, the court held that the limitation 'to substantially increase the efficiency of the compound as a copper extractant' was definite in view of the general guidelines contained in the specification. *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). A similar result was also seen in *Andrew Corp. v. Gabriel Electronics*, 847 F.2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988), where the Court held that the limitation 'which produces substantially equal E and H plane illumination patterns' was definite because one of ordinary skill in the art would know what was meant by 'substantially equal.' It is Applicants position, that in this case, the term substantially is being used consistent with the usage in *Mattison* and *Andrew Corp.* Accordingly, it is urged that claim 40 is definite and reconsideration and withdrawal of this rejection are respectfully requested.

6. The Examiner alleges that in claims 42-45, it is not clear what is being further limited other than intended use of the antibody.

Applicants disagree that the "functional language" in these claims are merely intended use and do not limit the claim, none the less, solely to expedite prosecution, applicants have canceled claims 42-45. Accordingly, this rejection is moot.

7. The Examiner alleges that in claim 55, "said PTN" protein lacks antecedent basis. Applicants have amended the claim to recite a PTN protein earlier in the claim thus obviating the lack of antecedent basis rejection. Accordingly, it is urged that claim 55 is definite and reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 102

8. The Examiner has rejected claim 52 under 35 U.S.C. 102(e)(1) as allegedly being anticipated by Jakobovits et al. (US 2002/0173629). Jakobovits et al. allegedly teach antibodies comprising the chains of SEQ ID NOs: 60 or 64 of the reference which comprises SEQ ID NO: 11 of the instant claim. Applicants respectfully traverse.

Applicants disagree, nevertheless, solely in order to expedite prosecution, claim 52 has been amended to comprise SEQ ID NOs: 5, 6, 7, 10, 11, and 12. Jakobovits et al. do not teach SEQ ID NOs: 5, 6, 7, 10, and 12. Therefore, Jakobovits et al. do not contain every element of the instant claims.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). "The identical invention must be shown in as complete detail as is contained in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, Jakobovits et al. do not contain every element of the instant claims. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e)(1) are respectfully requested.

9. Claim 55 is rejected under 35 U.S.C. §102(e)(2) as allegedly being anticipated by Paliard et al. (US Patent 6,562,346). Paliard et al allegedly teach the elicitation of monoclonal antibodies by immunization of a mammal with fusion proteins comprising a protein of interest and at least one T cell epitope, hybridization of B cells obtained from the immunized animal to a myeloma cell, and identification and culture of relevant hybridomas.

Applicants respectfully disagree, nevertheless, solely in order to expedite prosecution, claim 55 has been amended to recite a PTN protein. Paliard et al. do not teach PTN proteins. Therefore, Paliard et al. do not contain every element of the instant claims. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e)(2) are respectfully requested.

Rejections under 35 U.S.C. § 103(a)

10. Claims 39-46, 49-50 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jäger et al. (Int. J. Cancer 73: 537, 1997), Rauvala (EMBO J. 8:2933), Ledoux et al. (J. Histochem. Cytochem. 45: 1239, 1997), Harlow et al., Knight (US 5,675,063), Czubayko et al. (J. Biol. Chem. 269: 21358, 1994). Jäger et al. allegedly teach a polyclonal antibody to PTN, raised in rabbits by the methods of Rauvala, which inhibits the biological activity of the protein. As taught by Rauvala, the antibody was raised by immunization with the N-terminal peptide of PTN. Ledoux et al. allegedly teach polyclonal antibodies to PTN raised in rabbits. Harlow et al. allegedly teach that, once the sequence of a protein is known, it is routine and conventional in the art to elicit antibodies to peptides and/or fusion proteins derived from the protein and/or to prepare a bank of site-specific monoclonal antibodies for a variety of uses. Harlow et al. further allegedly teach rationales for the selection of synthetic peptides as immunogens. Knight allegedly teaches the 240E cell line as a fusion partner generally for producing rabbit monoclonal antibodies to a predetermined immunogen. Czubayko et al. allegedly desire antibodies as a specific drug for blocking the growth factor activity of PTN. The Examiner argues that one of ordinary skill in the art would have had a reasonable expectation of success and obvious motivation for generating monoclonal antibodies reactive with PTN for use as blocking agents in view of the cited references. Applicants respectfully traverse.

A determination of obviousness is not based on what a person skilled in the art might try or find obvious to try. The standard for rendering a claimed invention obvious is that the prior art must

suggest to those of ordinary skill in the art that they should have made the claimed invention and that they would have had a reasonable expectation of success in so doing. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In the present case, the Examiner has merely asserted, without evidence, that one of skill in the art would have had a reasonable expectation of success in obtaining neutralizing monoclonal antibodies to PTN. One of skill in the art would readily appreciate that there are differences between polyclonal and monoclonal antibodies. It is possible that multiple antibodies are required for the neutralizing activity of a polyclonal antibody. There is no basis to assert or assume *a priori* that because a neutralizing polyclonal antibody exists that a neutralizing monoclonal antibody can also be produced. None of the cited secondary references discuss the production of neutralizing monoclonal antibodies as being routine. In fact, applicants used a number of strategies to attempt to generate neutralizing monoclonal antibodies such as the use of T cell epitopes and autoimmune mouse strains after initial attempts failed to produce any neutralizing antibodies (see instant specification page 42, lines 3-31). This suggests that the production of a neutralizing monoclonal antibody to PTN was not the result of routine experimentation. The references cited by the Examiner were published in 1997 or earlier, well before the priority date of the instant application. If only routine experimentation was necessary to produce neutralizing monoclonal antibodies to PTN based on the polyclonal antibody of Jäger et al. and the desire for monoclonal antibodies of Czubyko et al., it seems likely that there would not have been such a long period of time where no one else made neutralizing monoclonal antibodies to PTN.

Prior to Applicants' disclosure, one of skill in the art would not have had a reasonable expectation of success in applying the teachings of Jäger et al. to develop a neutralizing monoclonal antibody to PTN as required by the pending claims. Therefore, the Examiner has failed to make a *prima facie* case that Jäger et al. renders the claimed invention obvious because not all the elements of the claimed invention are found within the teachings of Jäger et al. and one of ordinary skill in the art would not have a reasonable expectation of success based on the cited art. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

11. Claims 39-46, 49-50 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jäger et al. (Int. J. Cancer 73: 537, 1997), Rauvala (EMBO J. 8:2933), Ledoux et al. (J.

Histochem. Cytochem. 45: 1239, 1997), Harlow et al., Roes et al. (J. Immunol. Meth. 183:231-237, 1995), Amet et al. (Mol. Cell. Neurosci. 17: 1014, 2001), Czubayko et al. (J. Biol. Chem. 269: 21358, 1994). Roes et al. allegedly disclose immunization of knockout mice with the knockout gene product for production of monoclonal antibodies. Amet et al. allegedly disclose PTN knockout mice. Applicants respectfully traverse.

Roes et al. and Amet et al. do not make up for the deficiencies of Jäger et al. Given that Jäger et al. Rauvala, Ledoux et al., Harlow et al., Knight, Czubayko et al., Roes et al. and Amet et al. fail to teach or suggest each and every element of the claimed invention, the combination of references fail to render the claimed invention obvious. Reconsideration and withdrawal of this rejection are respectfully requested.

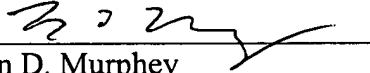
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants believe no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. GUH-026-101 from which the undersigned is authorized to draw.

Dated: September 17, 2008

Respectfully submitted,

By 
Ryan D. Murphey

Registration No.: 61,156
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant